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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/087,573	02/28/2002	Theodorus Petrus Maria Schetters	I 2001.004 US	3895
31846	7590	01/26/2004	EXAMINER BASKAR, PADMAVATHI	
			ART UNIT	PAPER NUMBER
			1645	

DATE MAILED: 01/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	SCHETTERS ET AL.
Examiner	Art Unit
Padmavathi v Baskar	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 24 October 2003.

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 32-35 and 64-67 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 32-35 and 64-67 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) The translation of the foreign language provisional application has been received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) Notice of References Cited (PTO-892) 4) Interview Summary (PTO-413) Paper No(s). _____.
2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) Notice of Informal Patent Application (PTO-152)
3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4/15/02. 6) Other:

DETAILED ACTION

1. Applicant's response to restriction filed on 10/24/03 is acknowledged. Claims 1-31 and 36-63 are canceled. New claims 64-67 have been added. Claims 32-35 and 64-67 are pending in the application.

Priority

2. This application claims priority to EUROPEAN PATENT OFFICE (EPO) 01200816.5 06/03/2001. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d) or (f), which papers have been placed of record in the file.

Information Disclosure Statement

3. Information Disclosure Statements filed on 4/15/02 acknowledged and a signed copy of is attached to this Office action.

Election

4. Applicant's election of Group II claims 32-35 drawn to protein 10/24/03 is acknowledged. Claims 32-35 and newly added claims 64-67, drawn to protein are included in Group II invention and accordingly under prosecution.

Specification Informalities

5. This application is informal in the arrangement of the specification. Applicant attention is directed to MPEP 608.01(a). For example: figures legends should be under Brief Description of Drawings.

Claims shoud begin with "I claim" or "we claim" or "What is claimed is".

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as Follows:
Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 32-35 and 64-67 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. The product, *Babesia canis* as claimed, has the same characteristics as that found in nature. To overcome this rejection the Examiner suggests the amendment of the claims to include purity limitations, which would distinguish the characteristics of applicant's product from the product, as it exists in nature. It is further suggested that such limitation include the terminology " purified and isolated" (i.e. if such purity is supported in the specification) and/or a description of what applicant's protein is "free of" relative to the natural source. (see Farbenfabriken of Elberfeld Co. v. Kuehmsted, 171 Fed. 887, 890 (N.D. Ill. 1909) (text of claim at 889); Parke-Davis & Co. v. H.D. Mulford Co., 189 Fed. 95, 103, 106, 965 (S.D.N.Y. 1911) (claim 1); and In re Bergstrom, 427 F.2d 1394, 1398, 1401-1402 (CCPA 1970).

Claim Rejections - 35 USC 112, first paragraph

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
8. Claims 32-35 and 64 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is referred to the interim guidelines on written description published June 15, 1998 in the Federal Register at Volume 63, Number 114, pp 32639-32645 (also available at www.uspto.gov). This is a written description rejection.

The claims are directed to a Babesia canis associated protein said protein having a molecular weight of 15 kD and comprising an amino acid sequence that is at least 80%, 85%, 90% and 95% homologous to the amino acid sequence as depicted in SEQ ID NO: 2 or an immunogenic fragment of said protein. Claims are also directed to a vaccine for combating Babesia canis infections comprising a nucleic acid sequence encoding a protein having a molecular weight of 15 kD and comprising an amino acid sequence that is at least 80% homologous to the amino acid sequence as depicted in SEQ ID NO:2 or an immunogenic fragment of said protein, a pharmaceutically acceptable carrier, an adjuvant and an additional protein derived from a virus or microorganism pathogenic to dogs or a nucleic acid sequence encoding said antigen wherein said virus or micro-organism pathogenic to dogs is selected from the group of Ehrlichia canis, Babesia gibsoni, vogeli, rossi, Leishmania donovan complex, Canine parvovirus, Canine distempervirus, Leptospira interrogans serovar canocola icterohaemorrhagiae, pomona, grippotyphosa , grippotyphosa, bratislava, Canine hepatitisvirus. Canine parainfluenzavirus, rabies virus,Hepatozoon canis and Borrelia burgdorfiri.

The specification discloses a recombinant Babesia canis protein having 15KD molecular weight and comprising the amino acid sequence as set forth in SEQ.ID.NO: 2. However, the specification does not disclose

- (1) Babesia canis protein having a molecular weight 15KD and comprising an amino acid sequence that is at least 80%, 85%, 90% or 95% homologous to the amino acid sequence as depicted in SEQ.ID.NO: 2 or an immunogenic fragments of said protein
- (2) A vaccine for combating B.canis infection comprising a Babesia canis protein having a molecular weight of 15KD and comprising an amino acid sequence that is at least 80%, homologous to the amino acid sequence as depicted in SEQ.ID.NO: 2 or an Immunogenic

fragments of said protein (the examiner is considering these as variants and address them as variants hereafter in the action)

Therefore, or said variants do not meet the guidelines on written description.

The specification fails to disclose any substitution, insertion or deletion or change in (i) a in a protein SEQ.ID.NO: 2 to obtain a variants having 80%, 85%, 90% or 95% homologous to the amino acid sequence as depicted in SEQ.ID.NO: or immunogenic functional fragments, (ii) a vaccine comprising said variants or a nucleic acid encoding said variants and an additional protein derived from a virus or microorganism pathogenic to dogs or a nucleic acid sequence encoding said antigen wherein said virus or micro-organism pathogenic to dogs is selected from the group of Ehrlichia canis, Babesia gibsoni, vogeli, rossi, Leishmania donovan complex, Canine parvovirus, Canine distempervirus, Leptospira interrogans serovar canocola icterohaemorrhagiae, pomona, grippotyphosa , grippotyphosa, bratislava, Canine hepatitisvirus. Canine parainfluenzavirus, rabies virus, Hepatozoon canis and Borrelia burgdorfiri.

The specification does not describe any variants in vaccine preparations for combating B.canis infection in dogs. None of the above variants and their use in a vaccine preparation meet the written description provision of 35 U.S.C. 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

Thus, the specification fails to teach variants sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed.

9. Claims 32-35 and 64 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated Babesia canis associated protein and a vaccine composition comprising a molecular weight of 15 KD and comprising the amino acid sequence SEQ ID NO: 2, does not reasonably provide enablement for Babesia canis protein having a molecular weight 15KD and comprising an amino acid sequence that is at least 80%, 85%, 90% or 95% homologous to the amino acid sequence as depicted in SEQ.ID.NO: 2 or an immunogenic fragments of said protein .

Claims are discussed supra.

The specification fails to provide an enabling disclosure other than protein SEQ.ID.NO: 2 itself because it fails to provide any guidance regarding how to make and use a protein that vary by 80%, 85%, 90% or 95% homologous to the amino acid sequence as depicted in SEQ.ID.NO: 2 or an immunogenic fragments of said protein.

The instant claims are evaluated for enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed.Circ.1988) as follows:

(1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the disclosed invention is relates to cloning of nucleic acid sequences encoding a novel Babesia canis associated proteins from B.canis isolate A and B from France that are useful for diagnostic tools for the detection of Babesia canis and for a vaccine composition against B.canis homologous strains

The specification on pages 19-36 indicates that the claimed protein may be used as diagnostic reagent and a vaccine composition against homologous *B.canis* infections. The specification, however, provides no working examples demonstrating (i.e., guidance) enablement for any protein that vary by 80%, 85%, 90% or 95% homologous to the amino acid sequence as depicted in SEQ.ID.NO: 2 or an immunogenic fragments of said protein. Any substitution, insertion or deletion or change in a peptide encoded by a nucleotide sequence of SEQ.ID.NO: 2 are highly complex and unpredictable. As taught by the prior art that even a single amino acid change in a protein leads to unpredictable changes in the biological activity of the protein. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological-activity of the protein (Burgess et al., *The Journal of Cell Biology*, 111:2129-2138, 1990). Thus, it is apparent that change in a peptide leads to loss of binding property of that peptide. Furthermore, it is unclear whether protein that vary by 80%, 85%, 90% or 95% homologous to the amino acid sequence as depicted in SEQ.ID.NO: 2 or an immunogenic fragments of said protein can be used as diagnostic reagent or in a vaccine composition. Thus, protein that vary by 80%, 85%, 90% or 95% homologous to the amino acid sequence as depicted in SEQ.ID.NO: 2 or an immunogenic fragments of said protein at protein level or nucleotide level and fragments must be considered highly unpredictable, requiring a specific demonstration of efficacy on a case-by-case basis.

The specification fails to provide an enabling disclosure for using protein that vary by 80%, 85%, 90% or 95% homologous to the amino acid sequence as depicted in SEQ.ID.NO: 2 or an immunogenic fragments of said protein because it fails to provide guidance protein that vary by 80%, 85%, 90% or 95% homologous to the amino acid sequence as depicted in SEQ.ID.NO: 2 or an immunogenic fragments of said protein is related to anti-microbial action

and its use in diagnostic or prophylactic reagent. The specification provides no disclosure how a protein variant of SEQ.ID.NO: 2 may be used as a vaccine because it fails to provide guidance whether this variant has the ability to induce a protective immune response or to bind to antisera from infected animal. Absent such demonstration, the invention would require undue experimentation to practice as claimed.

Claim objections

10. Claims 65-67 objected as being depended from canceled claims 36 and 38. Applicant is advised to amend the claims.

Rejections - 35 USC 112, second paragraph

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

12. Claims 32-35 and 64 –67 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 32 is vague and indefinite in the recitation of " 15 kD" In consideration of the discrepancies often encountered in the art between protein molecular weights when determined by different methods, whenever a molecular weight is recited to characterize a protein the claim should include not only the method by which it was determined, e.g. whether by sodium dodecyl sulphate polyacrylamide gel electrophoresis, gel filtration or some other method, but also whether the determination was made under denaturing or non-denaturing conditions and whether reducing or non-reducing conditions were used.

Claim 66 is rejected as being vague and indefinite in the recitation of "derived". Is this antigen isolated from a virus or microorganism?

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) The invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 32-35 and 64 are rejected under 35 U.S.C. 102(b) as being anticipated by Kulakov et al 1998 Molekulyarnaya Genetika, Microbiologiya i virusologiya (2), 7-13 (abstract only)

Claims are discussed supra.

The teachings of Kulakov et al 1998 disclose that cell lysates from various Brucella (i.e., Babesia) species including B.canis comprise 90-16KD antigens when analysed on immunoblotting (SDS-PAGE) using specific anti-rabbit sera. In the absence of evidence to the contrary the disclosed prior art cell lysate comprises B.canis associated protein 15KD antigen and characteristics such as SEQ.ID.NO: 2 is considered as an inherent property of the disclosed cell lysate. Since the Office does not have the facilities for examining and comparing applicants' product with the product of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594.

Vaccine is considered as an intended use of the B.canis protein. Cell lysate inherently contains pharmaceutical carrier. The prior art anticipated the claimed invention.

15. Claims 32-35 and 64 –65 are rejected under 35 U.S.C. 102(B) as being anticipated by Schetters et al 1992 (PARASITE IMMUNOLOGY 1992, 14(3) 295-305 abstract only).

Claims are discussed *supra*.

Schetters et al disclose a vaccine comprising Babesia associated protein in culture supernatants of Babesia canis in the adjuvant (see abstract). In the absence of evidence to the contrary the disclosed prior art culture supernatants comprises B.canis associated protein 15KD antigen. Characteristic such as SEQ.ID.NO: 2 is considered as an inherent property of the disclosed culture supernatants. Since the Office does not have the facilities for examining and comparing applicants' product with the product of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594. Thus the prior art anticipated the claimed invention.

Status of Claims

16. No claims are allowed.
17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padma Baskar whose telephone number is (703) 308-8886. The examiner can normally be reached on Monday through Friday from 6:30 AM to 4 PM EST

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Padma Baskar Ph.D

1/21/04.


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